Clinical Investigator Training Course

Investigator Responsibilities in Biomedical Research
Covered by FDA Regulations

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Objectives

Discuss Clinical Investigator Obligations according to FDA Regulations

Discuss Challenges That Arise in a System of Shared Responsibility

Discuss FDA’s Bio monitoring Research Program and How to Survive an Inspection
Starting Point

Standards for clinical care of patients ≠ Standards for academic research ≠ Standards for FDA regulated research
Clinical Trial Environment

- Investigator
- Sponsor
- Institution
- IRB
- State
- US FDA
- OHRP
- Study Subjects
Federal Legal Framework

- **Federal Food Drug and Cosmetic Act**
  - Section 505(i) is the statutory authority for the FDA’s oversight of clinical investigations to test safety and effectiveness

- **Code of Federal Regulations (CFR)**
  - Describe FDA’s authority over the conduct of clinical investigations
  - Sponsor/Investigator responsibilities
Clinical Trial Regulations

- Code of Federal Regulations
  - 21CFR11 Electronic records and Signatures
  - 21CFR50 Informed Consent
  - 21CFR54 Financial Disclosure
  - 21CFR56 IRB
  - 21CFR312 Investigational New Drug Applications
  - 21CRF812 Investigational Device Exemptions
Good Clinical Practice

GCP is a living standard and concept and therefore is continually being affected by evolving thoughts and standards

There is no perfect Knowledge of GCP!!!!
Good Clinical Practice

GCP is a complicated evolving discipline that intersects with several other complex evolving disciplines, including ethics, medicine and nursing, health systems, regulatory, administrative and case law, information technology, biostatistics, risk analysis, and health policy...to name a few.
ICH GCP and FDA GCP
ICH Guidelines

ICH Guidelines are joint guidelines issued by three regions (US, EU, and Japan)

- They reflect the current thinking in these regions

NOTE: Some countries place a little more or less emphasis on the guidelines. If performing international research you must understand the rules of each region.
ICH-1996

Good Clinical Practice (GCP)

- A standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected. (ICH E6)
FDA GCP

- Collection of related regulations and guidelines that, when taken together, define the clinical study-related responsibilities of sponsors, clinical investigators, monitors, institutional review boards and others involved in the clinical research process
FDA GCP

Code of Federal Regulations

- 21CFR11 Electronic records and Signatures
- 21CFR50 Informed Consent
- 21CFR54 Financial Disclosure
- 21CFR56 IRB
- 21CFR312 Investigational New Drug Applications
- 21CRF812 Investigational Device Exemptions
Why Does This Matter

FACT: FDA officials emphasize that agency inspectors will inspect sponsors, monitors, and investigators exclusively for compliance with FDA GCP regulations regardless of the GCP standard implemented in the trial.
GCP and Devices

- CDRH has not formally recognized ICH Guidance in that they have not issued the guidance from the division but they do support adherence to the principles.

- A more relevant guideline for Device Studies is ISO 14155:2011 – Clinical Investigation of Medical Devices for Human Subjects - GCP.
FDA Clinical Trial Guidance

- Generally cuts across all divisions—represent FDA’s current thinking on Good Clinical Practice and the conduct of clinical trials.

- All available at www.fda.gov/regulatoryinformation/guidances/ucm404975.htm
Available Clinical Trial Guidance

- 13 general information sheets
- 6 drug and biologic information sheets
- 5 Device information sheets
- 13 general guidance documents
- 8 IRB guidance documents
- 16 Drugs and biologic guidance documents
- 6 Medical device guidance documents
- 3 Electronic records guidance
- 3 Manufacturing guidance
- Approximately 13 draft guidance documents
THE STATE

Welcome to California
California Health & Safety Code

- §24172 - Experimental Subjects Bill of Rights
- § 24173 – Informed Consent
- § 24174 - Medical Experiment – pertains to drugs and devices
- § 24175 – Medical Experiments; informed consent
- § 24176 – Violations; damages; misdemeanor; waiver of rights
California Health & Safety Code

§ 24176 – Violations; damages; misdemeanor; waiver of rights

- Negligent failure to obtain ICF – Liable up to $1000.00
- Willful failure to obtain ICF – liable up to $5000.00
- Willful failure to obtain ICF which exposes the subject to a known substantial risk – misdemeanor or fine of $10,000
- Any representative or employee of a pharmaceutical company who has knowledge of risks or hazards and withholds the information – misdemeanor and/or $10,000 fine
The Institution

STANFORD
Belmont report

California Law: Protection of Human Subjects in Medical Experimentation Act

FDA: Food and Drug Administration

- Informed Consent (guidance)
- 21 CFR Part 50 - Protection of Human Subjects
- 21 CFR Part 56 - Institutional Review Boards
- 21 CFR Part 312 - Investigational New Drug Applications (INDs)
- 21 CFR Part 812 - Investigational Device Exemptions (IDEs)
- Information Sheet Guidances for IRBs, Investigators and Sponsors
  - Significant Risk and Nonsignificant Risk Medical Device Studies
- IRB Frequently Asked Questions
- Clinical Trials and Human Subject Protections - Guidance, resources, good clinical practices (GCPs)

OHRP: Office of Human Research Protections

- Title 45 CFR 46: Protection of Human Subjects
- Policy guidance and documents
- Inclusion of Children - Policy Implementation (NIH)
- Certificates of Confidentiality
- International Compilation of Human Research Protections - listing laws, regulations, and guidelines on human subjects research in over 100 countries, and standards from international and regional organizations
- OHRP Frequently Asked Questions

VA: Department of Veterans Affairs

- Office of Research & Development (ORD) Programs
- 38 CFR Part 16
- VA Handbooks website including:
  - VHA Handbook 1200.05 - Requirements for the Protection of Human Subjects in Research
  - VHA Handbook 1058.01 - Research Compliance Reporting Requirements
For Emphasis

- Federal Regulations
  - FDA Guidance pertains to the Federal Regulations
- State Regulations
- Local regulations
- FDA audits of sponsors, monitors, and Clinical Investigators based on FDA regulation only
Responsibilities in Clinical Research – According to FDA Regulations and supported by FDA Guidance
Who is an Investigator?

- An individual who actually conducts the clinical investigation (under whose immediate direction the drug is dispensed to a subject)
- If conducted by a team of individuals, the investigator is the responsible leader of the team. [21 CRF 321.3]
Sponsor-Investigator?

An individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed

- The term does not include any person other than the individual
- Both Sponsor and Investigator responsibilities [21 CFR 312.3]
Investigator Responsibilities

- Ensure investigation is conducted according to the
  - Signed investigator agreement (1572 or Investigator agreement with respect to device)
  - Investigational plan (re. PROTOCOL)
  - Applicable regulation

- Protecting the right, safety, and welfare of subjects under the investigators care

- Control of drugs (or devices) under investigation

- Ensuring that informed consent is adequately obtained according to 21 FR 50

- Ensuring IRB review, approval and reporting requirements are met per 21 CFR 56
Investigators Responsibilities

21 CFR 312.11

- An Investigator shall administer the drug only to subjects under the investigator’s personal supervision OR
- Under the supervision of a sub-investigator responsible to the investigator

THIS IS A VERY IMPORTANT STATEMENT
Investigator Responsibilities

- Control of investigational drug (312.61)
- Record Keeping and retention
  - Maintain adequate records of the disposition of the drug
  - Accurate case histories that record all observations, and
  - Other data pertinent to the investigation on each individual administered the investigational drug or employed as a control

- An investigator is required to maintain investigation records for:
  - 2 years following the date a marketing application is approved for the drug for the indication which it is being investigated
  - 2 years after the investigation is discontinued and FDA is notified if no application is to be filed or if the application has not been approved for such indication
Investigator Responsibilities

- **Progress reports (312.64)**
  - Progress to sponsor
  - Safety reports
    - Immediately report serious adverse events
    - Record non serious adverse events and report them to the sponsor according to the timetable for reporting specified in the protocol. **DO** clarify with the Sponsor what items are considered adverse events as we find the definition can get messy. (especially when inexperienced persons are employed on the study)
  - Final report to sponsor

- **Financial disclosure to sponsor (21 CFR 54)**
Investigator Responsibilities

Guidance (CDER, CBER, CDRH)

FDA final guidance document issued October 2009

- Guidance covers:
  - Appropriate delegation of study tasks
  - Appropriate training of study staff
  - Supervision of staff, including contracted personnel
  - Subject protections, including necessary medical care
IRB Review

- FDA Guidance (Including ICH E6) require submission of:
  - Consent documents
  - Protocol/amendments
  - Advertisements
  - Written information provided to the subjects
  - Investigators brochure
  - Investigators CV and/or qualifications
  - Progress reports and reports of injuries
Supervision

- For both Drugs and Device the investigator commits themselves to personally conduct or supervise the investigation

  - Note: FDA Knows “It is common practice for PI to delegate certain study tasks to employees, colleagues, or other third parties (individuals who are not under the direct supervision of the PI)”

Source – 2009 guidance
Supervision

- When the tasks are delegated by the PI, the PI is responsible for providing adequate supervision of those to whom tasks are delegated.
- The PI is accountable for regulatory violations resulting from failure to adequately supervise.

Source – 2009 guidance
Appropriate Delegation

- Any individual to whom a task is delegated must be qualified by education, training, and experience (and state licensure where relevant)
- Individuals delegated must meet any protocol specified requirements
- Listing of tasks and individuals delegated should be maintained

Source – 2009 guidance
Appropriate Delegation

- Appropriate delegation is more of an issue for tasks considered to be clinical or medical in nature
  - Evaluating study subjects to assess clinical response
  - Providing medical care during the study
Delegation Issues and Discussion

- FDA common observations –
  Individuals not qualified to conduct:
  - Screening evaluations (incl. Medical history and assessment of inclusion/exclusion criteria)
  - Physical exams
  - Evaluation of adverse events
  - Assessment of primary study endpoints
  - Obtaining informed consent

Source – 2009 guidance
Common Mistake Areas

- Medical History
- Relevant Medical History
- Concomitant Medications
- Adverse events vs. Current medical conditions
- Lack of understanding of primary endpoints and how the protocol supports them
FDA Observations - Supervision

- Factors that affect ability to provide adequate supervision
  - Inexperienced study staff
  - Demanding workload of study staff
  - Complex trials
  - Large number of subjects enrolled at site
  - Subject population is seriously ill
FDA Observations - Supervision

- Conducting multiple studies concurrently
- Conducting study from remote locations
- Conducting a study at multiple sites under oversight of single investigator
Helpful Hints: Have a PLAN

- Routine meetings with staff
- Routine meetings with monitors – YES I said that
- Procedures for correction and documentation of problems identified by study personnel
- Procedures for ensuring proper consent
- Procedures for ensuring data accuracy
Have a PLAN - continued

- Procedures for dealing with data queries – (this can be challenging between sponsors so you dictate the plan to them!)
- Procedures for ensuring compliance with protocol, adverse event assessment and reporting requirements
- Procedures for addressing medical and ethical issues
Investigator Responsibilities

FOLLOW THE PROTOCOL

- Failure to follow the protocol (otherwise known as protocol deviations or violations) has been on FDA’s top ten list ever since the BIMO inspection program started in 1977. Last year this was an issue in almost 40% of the inspections.
Violations/Deviations

- Prospective action before making a deviation is preferred.
  - Call Sponsor and the IRB
- Violations after the fact should be identified immediately
- Violations/deviations can cause harm to the subject and/or make it difficult to assess the study endpoints
Investigator Responsibilities

Subject protections, including necessary medical care

- Reasonable medical care for study related medical problems
- Provision of access to appropriate medical care when specialized care is required
- Adherence to study protocol is also considered a protection with respect to not exposing subject to unreasonable medical risks
- Protocol violations – can also be considered failure to protect
Regulatory Documents

THE FACTS
Statement of Investigator
Form FDA 1572

What is it?

- This is an agreement signed by the investigator to provide certain information to the sponsor and assure that he/she will comply with the FDA regulations related to the conduct of a clinical investigation of an investigational new drug or biologic.

NOTE: This form is NOT used for studies involving devices.
# The 1572

The 1572 is a form used by the Department of Health and Human Services, Food and Drug Administration. It is used to provide a statement of investigator details. The form includes sections for:

1. **Name and Address of Investigator**
   - Name of Principal Investigator
   - Address 1
   - City, State/Province/Region, Country, ZIP or Postal Code

2. **Education, Training, and Experience**
   - Qualification as an expert in the clinical investigation of the drug for the use under investigation. Selection of one of the following:
     - Curriculum Vitae
     - Other Statement of Qualifications

3. **Name and Address of Any Medical School, Hospital, or Other Research Facility Where the Clinical Investigation(s) Will Be Conducted**
   - Name of Medical School, Hospital, or Other Research Facility
   - Address 1
   - City, State/Province/Region, Country, ZIP or Postal Code

4. **Name and Address of Any Clinical Laboratory Facilities to Be Used in the Study**
   - Name of Clinical Laboratory Facility
   - Address 1
   - City, State/Province/Region, Country, ZIP or Postal Code

5. **Name and Address of the Institutional Review Board (IRB) That Is Responsible for Review and Approval of the Study(es)**
   - Name of IRB
   - Address 1
   - City, State/Province/Region, Country, ZIP or Postal Code

6. **Names of Subinvestigators**
   - If not applicable, enter "None"

7. **Name and Code Number, If Any, of the Protocol(s) in the IND for the Study(es) to Be Conducted by the Investigator**

The form is used to ensure that all necessary details are provided for the clinical investigation of a drug. It is important for ensuring compliance with regulatory requirements.
The 1572
Device Studies?

- The sponsor should develop an investigators agreement which includes the elements of 21 CFR 812.43(c).
- Very similar language to the form FDA 1572
- The sponsor should have all investigators sign the agreement prior to participating in the study.
CVs

- CVs for PI is required to show proper education and training to perform the study.
- CV’s for sub-investigators are collected to ensure that they are qualified to perform their functions with respect to the clinical investigation.
- CV’s do not have to be signed and dated. It is not a requirement.
Other Regulatory Documents

- Financial disclosure
- IRB Information
- Lab Information
- PI license - If applicable
- Protocol/amendment signature pages
- IRB approvals of study and associated documents/processes
Sponsor Responsibilities

- Select qualified investigators (21 CFR 312.50)
- Design, conduct, perform, monitor, audit, record, analyze, and report clinical trials such that they can provide assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects have been protected.
FDA’s Responsibilities In Regulated Research

- Protect the rights and welfare of human research subjects
- Assure the quality and integrity of bioresearch data
- Ensure compliance with regulatory requirements
Moral of the Story

It takes a village
IN ADDITION TO ISO 9000, WE WILL STRIVE TO BE QS-9000 COMPLIANT.

THAT MEANS FALSIFYING THE FOLLOWING DOCUMENTS: QSR, APQP, FMEA, MSA, SPC, PPAP AND QSA.

REMEMBER, YOU CAN'T SPELL COMPLIANCE WITHOUT "LIANCE."
Section II

THE FDA AUDIT
FDA Oversight

BIMO Inspection Program

In 1977 the Bioressearch Monitoring Inspection Program was developed to assure quality and integrity of data and to determine that the human rights and welfare of human and animal subjects are adequately protected.
FDA Bio-research Monitoring Program

- Inspections of clinical investigators, sponsors, IRB, GLP facilities and Bioequivalence studies
  - Investigator shall permit the FDA to have access to, and copy and verify any records or reports made by the investigator (312.68)

- Types of Inspections
  - Data validation in support of new drug application (NDA) or PMA
  - For Cause (compliance)
  - Surveillance
# BIMO Inspections -2013

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BIMO Inspection Program

- Compliance Guidance Program Manual – The SOP for Inspections
- 21 CFR 11
- 21 CFR 50
- 21 CFR 54
- 21 CFR 56
- 21 CFR 312
- 21 CFR 812
- 21 CFR 314 and 814 – NDA and PMA
The Process

- Notice of Inspection – Inspections can be announced or unannounced
- Clinical Investigators must allow FDA to access, copy, and verify any records or reports made by the CI with regard to, among other records, the disposition of the investigational product and subject case histories
Typical FDA Inspector Questions During Interview

- Delegation of Authority – who, when, where
  - Screening of subjects
  - Interpreting screening results/admitting to the study
  - Informed consent of subjects (the process)
  - Receipt of test article; handling; administration; return
  - Reporting (including safety reporting)/transcribing data
  - Clinical Laboratory (who evaluates the results? when?)
  - Training (Is this real training or just for show?)
  - Archiving of study data
The FDA Inspection is not a scientific review of the data or the protocol.
During the Inspection

- **Do:**
  - Provide inspector with what they **ask** for.
  - Answer the inspector’s questions concisely and do not volunteer additional information.
  - Provide the inspector with adequate space.

- **DO NOT** provide documents or information that they do not ask for.
After The Inspection

FDA Inspector conducts an exit interview. Outcomes can be:

- No Action Indicated or
- If Inspector finds deficiencies with respect to regulations he/she issues a written Form FDA 483 (Inspectional Observations)
- If the Inspector is issuing a 483, this is the time to engage in a verbal discussion about the findings
Form FDA 483 Response

- Again - Engage in verbal discussion at closeout
  - This is not a blame session. As the PI is your responsibility to adhere to your obligations. The inspector is issuing findings based on what they have that was available to the PI.

- Send written response within 15 days
483 Response

The written response

- This is an opportunity to explain. In the event that the PI failed to adhere to the regulations, the Principle Investigator must submit a corrective action plan with real and specific corrective actions.
- ..We will do better next time will earn you a Warning letter
Most Common Deficiencies

- Same since the BIMO program started
  - Failure to follow the investigational plan and/or regulations (40%) – also know as Protocol violations/deviations
  - Inadequate record keeping (26%)
  - Inadequate accountability for the investigational product (9%)
  - Inadequate communication with the IRB (7%)
  - Inadequate subject protection – failure to report AEs and informed consent issues (1%)
Common Causes

- Poor supervision and training of study staff
- Insufficient investigator involvement in study conduct
- Inappropriate delegation of study tasks to unqualified persons
- Failure to adequately protect study subjects
- Overworked investigator and study staff (too many subjects, complex study with large data collection, too many concurrent studies)
FDA Compliance Classifications

- **NAI** – No Action Indicated

- **VAI** – Voluntary Action Indicated
  - Minor deviations(s) from regulations
  - Voluntarily correction is requested

- **OAI** – Official Action Indicated
  - Serious non-compliance requiring regulatory or administrative action by FDA
Clinical Investigator Inspections – FY 2013

FY'13 CI Inspections Classified*
All Centers

*inspections classified in FY’13 no matter when inspection occurred
Regulatory Actions

- Warning Letter
- Notice of Disqualification Proceedings and Opportunity to explain (NIDPOE)
- Disqualification
- Criminal investigations by Office of Criminal Investigations (OCI)
- Debarment
Case 1: Dr. Holland - Lax supervision

- Study Coordinator enrolled ineligible subjects in oncology trials
- Coordinator altered source records and created fraudulent CRFs to make subjects appear eligible
- Data manipulations should have been apparent to attentive clinician
- Subject who was ineligible due to poor renal and liver function was enrolled and died as a result
- Study coordinator sentenced to 71 months in prison and debarred from any future involvement in FDA regulated research
- Dr. Holland-5 years probation, $500k restitution, disqualified
JAILED PSYCHIATRIST PLEADS GUILTY AND IS SENTENCED ON
CHARGES OF FALSIFIED RECORDS OF CLINICAL TRIALS
INVOLVING CHILDREN

FOR IMMEDIATE RELEASE

DR. MARIA CARMEN PALAZZO, age 58, pled guilty in federal court today before U. S. District Judge Mary Ann Vial Lemmon to fifteen (15) counts of failing to prepare and maintain records, with intent to defraud and mislead, in connection with clinical trials to evaluate the efficacy and safety of Paxil in children and adolescents with Obsessive-Compulsive Disorder (OCD), announced U. S. Attorney Jim Letten.

According to court documents, PALAZZO, who specialized in psychiatry, was a clinical investigator for SmithKline Beecham d/b/a GlaxoSmithKline, was involved in two clinical trials evaluating Paxil’s safety and effectiveness in children and adolescents. Some of the study records indicated that PALAZZO included psychiatric diagnoses inconsistent with patients’ psychiatric histories; prepared multiple psychiatric evaluations on study patients which contained different diagnoses and treatment plans; reported symptoms of OCD when PALAZZO knew that the study subject did not demonstrate such symptoms; and reported that PALAZZO examined study subjects when she had not.

PALAZZO is currently serving an 87 month prison sentence after being convicted of 39 counts of health care fraud following a 12-day trial in April 2008. In the instant case, PALAZZO was sentenced to thirteen (13) months in prison to run concurrent to the previous sentence as well as serve one (1) year of supervised release during which time she will be under federal supervision and risk additional imprisonment should she violate any rules of the release. Additionally, PALAZZO was ordered to pay restitution to GlaxoSmithKline in the amount of $91,824 and $1,500 in special assessments.

The case was investigated by the Food and Drug Administration’s Office of Criminal Investigations, U. S. Department of Health and Human Services, Office of Inspector General, the Federal Bureau of Investigation and the Louisiana Medicaid Fraud Control Unit.

The case was prosecuted by Assistant U. S. Attorney Patrice Harris Sullivan, the Health Care Fraud Coordinator in this District.

(Download Factual Basis)
Case #2 – Dr. Palazzo

“...The defendant agreed to conduct Studies 704 and 716 in accordance with the protocol and to only make changes in the protocol after notifying the sponsor or, if necessary for the safety of the subject..."

The defendant also agreed to personally conduct or supervise the investigation and to maintain adequate and accurate records in accordance with 21 CFR §312.62, and to comply with all other obligations of clinical investigators found in 21 CFR 312.

At the bottom of each Form 1572 was a warning that statement on the form had to be truthful and if found not to be, could result in a prosecution for false statement to a government agency.
Case #2 - Palazzo

- Study records indicated that Dr. Palazzo
  - Included psychiatric diagnosis inconsistent with patients’ psychiatric histories;
  - Prepared multiple psychiatric evaluations on study patient which contained different diagnoses and treatment plans;
  - Reported symptoms of OCD when the study subject did not demonstrate such symptoms; and
  - Examined study subject when she had not

- Sentenced to thirteen (13) months in prison
Columbia University Medical Center
- Dr. Lobo as the Sponsor
- You failed to ensure proper monitoring including:
  - Failure to identify that the Investigator did not obtain informed Consent for 28 out of 50 subjects
  - Failure to identify that the IRB approval had lapsed from March 31 to June 3
  - Four subjects were not dosed according to the protocol
Warning Letters and the Corrective Action Plans

- Recent Warning letters have sited inadequate corrective action plans. (i.e. no real tangible plan)
  - Dr. Lobo – Columbia
  - Dr. Zimmerman - Columbia
  - Frazer
  - Byrzunski
How can clinical investigators ensure high quality data and subject safety?

- Create systems that limit opportunity for errors
- Select qualified staff and ensure adequate training and supervision
  - Ensure staff are not performing tasks they are not qualified to do (assessing eligibility, physical exams, assessing AEs)
  - Ensure oversight of sub investigators and study staff
How can clinical investigators ensure high quality data and subject safety?

- Implement system to detect and correct errors in real time
  - Pay attention to monitoring queries and respond promptly
  - Audit trail of changes should make clear what was changed, who changed it, and why it was changed
  - Evaluate need for system wide corrections and training
Improve Process – Be Proactive

- Address human factors in systems
  - Hire experienced, qualified staff
  - Avoid conflicts of interest/ financial incentives
  - Decrease number of times data are handled
  - Assess ability to comply with protocol visits; laboratory testing; electronic systems for data capture; archiving and transmission to sponsor; maintaining records; drug accountability
Improve Process – Be Proactive

- Create systems that limit opportunity for errors
  - Simplify protocol and outcomes assessed
  - Be realistic about the amount of data to be collected
  - Standardize systems and formats where possible
  - Use validated instruments/definitions
  - Write down all procedures
Improve Process - Be Proactive

- Don’t re-invent the wheel
- Keep amendments to a minimum and check CRFs and consent against each change
Improve Process

- Data and safety monitoring plan, data management plan, Quality Assurance Plan, Data Analysis Plan
- Insist on training and then test it
- Think carefully about un-blinding procedures
- Have weekly team meetings
- Audit yourself – be open and honest
Implement system to Detect Errors

- Do real time cleaning of the data
- Pay attention to monitoring queries and respond promptly – close the loops
- Audit trail of changes should make clear what was changed, who changed it, and why it was changed
- Evaluate the need for system wide corrections and training
Key Points

- Clinical Investigators play a key role in ensuring high quality studies.

- Good care of patients is not the same as Good Clinical Practice in research.
  - Ensure that all staff have a clear understanding of responsibilities under the FDA regulations.
At stake is the public confidence and participation in the clinical trials and ultimately the availability of safe and effective products.